Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (currently amended) A method of detecting whether a candidate polypeptide including a target epitope is in i) a wildtype conformation or ii) an aggregated or misfoldednon-wildtype conformation in a sample, comprising:

contacting the polypeptide with a blockingchemical modifying agent that chemically reacts with and selectively blocks accessible target epitope, wherein in the wildtype conformation, the target epitope is accessible and reacts with the blocking agent, and wherein in the aggregated or misfoldednon-wildtype conformation, the target epitope is inaccessible and the target epitope cannot react with the blocking agent;

removing the unreacted blockingchemical modifying agent from contact with the polypeptide;

modifyingdisaggregating or denaturing the candidate polypeptide to convert any inaccessible target epitope to accessible target epitope,

contacting the polypeptide with an aptamer or antibodydetection agent that binds selectively to the target epitope that was converted from inaccessible target epitope to accessible target epitope, wherein binding between detection agentthe aptamer or antibody and converted target epitope indicates that the candidate polypeptide was in an aggregated or misfoldednon-wildtype conformation and wherein lack of binding between the detection agentaptamer or antibody and the target epitope indicates that the polypeptide was in a wildtype conformation in the sample.

2. (currently amended) The method of claim 1, wherein the candidate polypeptide comprises prion protein, the wild type conformation comprises the conformation of wild type prion protein and the ~~non-wildtype~~aggregated or misfolded conformation comprises the conformation of PrP^{Sc}.

3. (withdrawn) The method of claim 1, wherein the candidate polypeptide comprises beta-amyloid polypeptide, tau protein or APP protein.

4. (withdrawn) The method of claim 1, wherein the candidate polypeptide comprises SOD1.

5. (withdrawn) The method of claim 1, wherein the candidate polypeptide comprises alpha-synuclein.

6. (withdrawn) The method of claim 1 wherein the candidate polypeptide comprises huntingtin protein.

7. (withdrawn) The method of claim 1, wherein the candidate polypeptide comprises p53.

8. (withdrawn) The method of claim 1, wherein the candidate polypeptide comprises islet amyloid polypeptide or resistin.

9. (currently amended) The method of claim 1, wherein the ~~blocking~~chemical modifying agent is selected from the group consisting of peroxynitrite, hydrogen peroxide, methylene compounds, succinic anhydride, epoxides, diethyl pyrocarbonate, 4-hydroxynonenal (4HNE) and diazirine.

10. (cancelled)

11. (previously presented) The method of claim 1, wherein the polypeptide is denatured by heat and/or detergent and/or chaotropic agents.

12. (currently amended) The method of claim 1, wherein the polypeptide is ~~modified~~disaggregated by treatment with a disaggregation agent to disaggregate the polypeptide from the aggregated polypeptides.

13. (original) The method of claim 12, wherein the disaggregation agent is selected from at least one of the group consisting of chaotropic agents, detergent and heat.

14. (original) The method of claim 13, wherein the detergent comprises SDS.

15. (cancelled)

16. (currently amended) The method of claim ~~15~~, wherein the aptamer or antibody is directed against a prion polypeptide epitope.

17. (previously presented) The method of claim 16, wherein the antibody comprises the antibody designated as 6H4 or the antibody designated as 3F4.

18. (withdrawn) The method of claim 15, wherein the aptamer or antibody is directed against an amyloid beta epitope.

19. (withdrawn) The method of claim 16, wherein the antibody comprises 6E10 or 4G8.

20. (currently amended) The method of claim 1, wherein the aggregated~~non-wildtype~~ conformation is indicative of a disease caused by protein aggregation.

21. (original) The method of claim 20, wherein the disease comprises prion disease.

22. (original) The method of claim 20, wherein the disease comprises BSE or CJD.

23. (withdrawn) The method of claim 20, wherein the disease comprises Alzheimer's disease.

24. (withdrawn) The method of claim 20, wherein the disease comprises Parkinson's disease or Lewy body disease.

25. (withdrawn) The method of claim 20, wherein the disease comprises Huntington's disease.

26. (withdrawn) The method of claim 20, wherein the disease comprises amyotrophic lateral sclerosis.

27. (withdrawn) The method of claim 20, wherein the disease comprises cancer.

28. (cancelled)

29. (currently amended) The method of claim 1, wherein prior to contacting the ~~blocking~~ chemical modifying agent with the candidate polypeptide, the target epitope is mapped.

30. (previously presented) The method of claim 1, wherein the polypeptide is in a postmortem or antemortem sample selected from the group consisting of CSF, serum, blood, urine, biopsy sample and brain tissue.

31. (withdrawn) A kit for detecting whether a candidate polypeptide including a target epitope is in i) a wildtype conformation or ii) a non-wildtype conformation, comprising a detecting agent that recognizes the target epitope and instructions for at least one of i) mapping a target epitope, ii) contacting a candidate polypeptide with a blocking agent, and iii) contacting a candidate polypeptide with a detecting agent.

32. (withdrawn) The kit of claim 31 wherein the detecting agent comprises an aptamer or an antibody.

33. (withdrawn) The kit of claim 32 wherein the antibody comprises 6H4, 3F4, 6E10 or 4G8, optionally immobilized to a solid support.

34. (withdrawn) The kit of claim 31, further comprising buffers and reagents for ELISA, including sandwhich ELISA, fluorescent ELISA.

35. (withdrawn) The kit of claim 31 further comprising a blocking agent.

36. (withdrawn) The kit of claim 31 further comprising a denaturing agent selected from at least one of the group of detergents and chaotropic agents.

37. (withdrawn) The kit of claim 31, further comprising a polypeptide standard.

38. (withdrawn) The kit of claim 34, wherein the polypeptide standard comprises a recombinant disease protein or a recombinant protein that mimics a disease protein.

39. (currently amended) A method of detecting whether a candidate polypeptide that has been contacted with a ~~blocking~~chemical modifying agent is i) a wildtype conformation or ii) an aggregated or misfolded~~non-wildtype~~ conformation, wherein the candidate polypeptide comprises at least one target epitope and, following contact with the ~~blocking~~chemical modifying agent and removal of the ~~blocking~~chemical modifying agent, the candidate polypeptide has been ~~modified~~disaggregated or denatured to convert any inaccessible target epitope to accessible target epitope, the method comprising:

contacting the polypeptide with an aptamer or antibody~~detection agent~~ that binds selectively to the target epitope that was converted from inaccessible target epitope to accessible target epitope, wherein binding between the aptamer or

antibody~~detection agent~~ and converted target epitope indicates that the candidate polypeptide was in an aggregated or misfolded~~non-wildtype~~ conformation and wherein lack of binding between the aptamer or antibody~~detection agent~~ and the target epitope indicates that the polypeptide was in a wild type conformation.

40. (withdrawn) The method of claim 1, wherein the target epitope is within the superoxide dismutase 1 polypeptide and the target epitope comprises all or part of the following amino acid sequences:

Gln Lys Glu Ser Asn Gly (SEQ ID NO:4);

Glu Asp Asn Thr Ala Gly Cys Thr Ser Ala (SEQ ID NO:5);

Pro Lys Asp Glu Glu Arg His Val (SEQ ID NO:6);

Ala Asp Lys Asp Gly (SEQ ID NO:7);

Gly Lys Gly Gly Asn Glu Gln Ser Thr Lys (SEQ ID NO:8);

Asp Leu Gly Lys Gly Gly Asn Glu Glu Ser Thr Lys Thr Gly Asn Ala Gly Ser (SEQ ID NO:9); or

Asn Pro Leu Ser Arg Lys His Gly Gly Pro Lys Asp Glu Glu (SEQ ID NO:10).

41. (currently amended) The method of claim 1, wherein binding between the ~~detection agent~~aptamer or antibody and the converted target epitope is detected using dissociation enhanced lanthanide fluoroimmunoassay and time-resolved fluorescence.

42. (withdrawn) An isolated polypeptide consisting of the amino acid sequence Asp Leu Gly Lys Gly Gly Asn Glu Glu Ser Thr Lys Thr Gly Asn Ala Gly Ser (SEQ ID NO:9).

43. (withdrawn) An isolated polypeptide consisting of the amino acid sequence Asn Pro Leu Ser Arg Lys His Gly Gly Pro Lys Asp Glu Glu (SEQ ID NO:10).

44. (withdrawn) A method of making an antibody specific for the isolated polypeptide according to claim 42.

45. (withdrawn) A method of making an antibody specific for the isolated polypeptide according to claim 43.

46. (withdrawn) An antibody specific for an epitope comprising an amino acid sequence selected from the group consisting of:

Asp Leu Gly Lys Gly Gly Asn Glu Glu Ser Thr Lys Thr Gly Asn Ala Gly Ser (SEQ ID NO:9); and

Asn Pro Leu Ser Arg Lys His Gly Gly Pro Lys Asp Glu Glu (SEQ ID NO:10).

47. (previously presented) The method of claim 1, wherein the target epitope is inaccessible because the candidate polypeptide is aggregated.

48. (currently amended) The method of claim 1, wherein the target epitope is inaccessible because the candidate polypeptide is ~~in an different conformation as compared to the wildtype conformation~~misfolded.

49. (currently amended) A method of detecting whether a candidate polypeptide including a target epitope is in i) a wildtype conformation or ii) an aggregated or misfolded~~non-wildtype~~ conformation, comprising:

contacting the polypeptide with a ~~blocking~~chemical modifying agent that chemically reacts with and selectively blocks accessible target epitope, wherein in the aggregated or misfolded~~non-wildtype~~ conformation, the target epitope is accessible and reacts with the chemical modifying~~blocking~~ agent, and wherein in the wildtype conformation, the target epitope is inaccessible and the target epitope cannot react with the chemical modifying~~blocking~~ agent;

removing unreacted chemical modifying ~~blocking~~agent from contact with the polypeptide;

~~modifying~~disaggregating or denaturing the candidate polypeptide to convert any inaccessible target epitope to accessible target epitope; and

contacting the polypeptide with an aptamer or antibody ~~detection agent~~that binds selectively to the target epitope that was converted from inaccessible target epitope to accessible target epitope, wherein binding between the aptamer or antibody ~~detection agent~~and converted target epitope indicates that the candidate polypeptide was in a wildtype conformation and wherein lack of binding between the aptamer or antibody ~~detection agent~~and the target epitope indicates that the polypeptide was in an aggregated or misfolded ~~non-wildtype~~conformation.

50. (withdrawn) The method of claim 20, wherein the disease comprises diabetes.

51. (currently amended) The method of claim 1, wherein prior to contacting the ~~blocking~~chemical modifying agent with the candidate polypeptide, the candidate polypeptide is ~~in a sample that is~~pretreated by one or more of the following methods: adsorption, precipitation, or centrifugation.

52. (New) The method of claim 1 wherein the chemical modifying agent chemically reacts with and selectively blocks the target epitope recognized by the antibody designated as 3F4 or the target epitope recognized by the antibody designated as 6H4.

53. (New) The method of claim 1 wherein the chemical modifying agent covalently reacts with the target epitope.

54. (New) The method of claim 11 where the chaotropic agent is selected from guanidine salts, urea or thiourea.

55. (New) The method of claim 13 wherein the chaotropic agent is selected from guanidine salts, urea or thiourea.

56. (New) A method of detecting whether a sample contains prion polypeptide (PrP) in a i) wildtype or ii) aggregated conformation, comprising:

contacting polypeptide in the sample with peroxynitrite to block accessible target epitope on the PrP, wherein in the wildtype conformation, the target epitope is accessible and reacts with the peroxynitrite, and wherein in the aggregated conformation, the target epitope is inaccessible and the target epitope cannot react with the peroxynitrite;

removing unreacted peroxynitrite from contact with the PrP;

disaggregating or denaturing the PrP to convert any inaccessible target epitope to accessible target epitope; and

contacting the sample with antibody that binds selectively to the target epitope that was converted from inaccessible target epitope to accessible target epitope, wherein binding between the antibody and the converted target epitope indicates that the PrP was in an aggregated conformation and wherein lack of binding there between indicates that the PrP was in a wildtype conformation.